REMARKS/ARGUMENTS

I. Status of the claims

No amendments were made. Claims 34-63 are pending. The Examiner has acknowledged that claims 50-63 are allowable.

II. Obviousness Rejections

A. Rejection over Gagnor et al. in view of Locatelli et al.

The Examiner rejected claims 34-41 as allegedly obvious in view of Gagnor *et al.* in view of Locatelli *et al.* According to the Examiner, Gagnor *et al.* describes a composition comprising ps-β-I and ps-α-II (which the Examiner argues represents a target and control nucleic acid, respectively) wherein the two nucleic acids comprise at least 8 or 10 nucleotides in length that are essentially parallel complementary. *See*, Office Action, page 3, second sentence. The Examiner further argues that Gagnor *et al.* describes a composition comprising "primers/probes and comprises a primer and/or probe binding sites for use in a RT-PCR reaction and hybridization reaction." *See*, Office Action, page 3, last sentence. The Examiner acknowledged that Gagnor *et al.* did not teach a thermostable polymerase or two sets of primers for the target and control nucleic acids. *See*, Office Action, page 3, next to last sentence. However, the Examiner argued that Locatelli *et al.* describes a composition comprising a target and control nucleic acid, primers for their amplification and a thermostable polymerase. Without any explanation of why or how one of skill in the art would do so, the Examiner argued that one of ordinary skill in the art would have been motivated to modify the compositions of Gagnor to encompass primers for both the target and control nucleic acid along with a thermostable polymerase in a single vessel as taught by Locatelli.

Applicants respectfully traverse the rejection. The Examiner has not set forth a motivation for why those of ordinary skill in the art would be motivated to combine the cited references.

As a first point, the Examiner is wrong in suggesting that the oligonucleotides ps-β-I and ps-α-II in Gagnor (*see*, office action, page 3, second sentence) are equivalent to the target and control nucleic acids as presently claimed. The claims require that the target and

control nucleic acids have at least 8 contiguous nucleotides that are essentially parallel complementary. Oligonucleotides ps-β-I and ps-α-II do not have 8 contiguous nucleotides that are essentially parallel complementary and therefore the rejection incorrectly characterizes the cited art.

Second, contrary to the Examiner's statements, Gagnor does not describe RT-PCR. Instead, Gagnor describes reverse transcription/RNAse H assays to assess binding competition of alpha and beta nucleic acid oligonucleotides. *See*, page 5109, paragraphs 1 and 2, and "Materials and Methods" section, particularly "RNase H digestions" and "Reverse transcription assay" sections. This is not a description of RT-PCR.

The Examiner relies on Gagnor teaching RT-PCR for the obviousness rejection. *See*, near the bottom of page 6 of the office action. As explained in Applicants' previous response, dated August 11, 2005, page 8, there is no evidence in the cited art that a polymerase could extend the short, alpha oligonucleotides described in Gagnor. According to the Examiner on page 6 of the Office Action, Gagnor teaches extension of oligonucleotides with a polymerase by teaching RT-PCR. As explained above, Gagnor does not in fact describe RT-PCR or that any polymerase would add nucleotides to the ends of the oligonucleotiodes described in Gagnor. Therefore, Applicants arguments in the last response still hold. There is no evidence that a polymerase would add nucleotides to the ends of the oligonucleotiodes described in Gagnor. If there is not even evidence that it would work, why would one of ordinary skill make the combination?

In a related point, there is no teaching or suggestion to use the oligonucleotides in Gagnor for amplification. The Examiner argues that because the claims are directed to a composition, and not a method, that the "for amplification" language in the claims is not a limitation because it is a "use". Applicants disagree on this point as not *any* primers are encompassed by the claims. Only those that would allow for amplification of the target or control nucleic acid under amplification conditions are encompassed by the claims.

Perhaps more importantly, the *art* must provide *some* reason for combining the references as the Examiner suggests to perform the claimed invention. As the claims include different primers, and primers are typically used in amplification, the Examiner must provide a

reasonable explanation for why those of ordinary skill in the art would perform an amplification (or alternatively some other reason) to combine the claimed components, including primers, in a composition. The Examiner has not done so.

The Examiner states that a composition comprising a target nucleic acid and a parallel complementary control nucleic acid is disclosed in Gagnor and discussed Figure 1 on page 5108 and 5110, first paragraph under "Results". The cited text in the "Results" section indicates that a parallel complementary alpha-oligonucleotide, by virtue of exhibiting the "non-natural" alpha-configuration at each anomeric carbon atom (see, page 5105, "Introduction", first paragraph and second paragraph, first sentence), does hybridize specifically (i.e., anneal) to a target sequence. This leads to the basic teaching of the document, namely that due to their capability of annealing, parallel complementary alpha oligonucleotides interfere with RNase H-mediated hydrolysis and reverse transcription of mRNA (*see*, title and abstract). If this teaching were applied according to the present invention, the result would be that parallel complementary alpha oligonucleotides would hybridize to their original target DNA and not to the control. This, of course, makes no sense. As used in the present invention, parallel complementary sequences do not hybridize. Gagnor teaches just the opposite and therefore attempts to uses Gagnor's alpha oligonucleotides in the present invention results in the opposite of the desired result, i.e., cross-hybridization of target and control.

Locatelli teaches the use of a target and control nucleic acid wherein the target and control do not hybridize to each other (*see*, Locatelli, paragraph spanning pages 4-5, teaching that "competition" between the target and "calibrator" nucleic acid should be reduced as much as possible so that a reaction is carried out in a single tube). If parallel complementary alpha oligonucleotides of Gagnor were used as the target and control nucleic acids, the control and target nucleic acids would hybridizing to each other, which is just the opposite of what Locatelli teaches! The combination of the two cited references, as the Examiner suggests, therefore does not make sense.

In short, the Examiner has not set forth a *prima facie* rejection because the prior art has been incorrectly characterized and because no motivation has been provided for why those of ordinary skill in the art would combine the references. Moreover, as explained herein,

any attempt at combination of the references does not result in the claimed invention but instead leads to nonsensical amplification of oligonucleotides for no apparent purpose and with the result that the target and control nucleic acids cross-hybridize, which is just the opposite of what Locatelli teaches. Accordingly, Applicants respectfully request withdrawal of the rejection.

B. Rejection over Gagnor et al. in view of Locatelli et al. further in view of Ahern et al.

The Examiner also rejected claims 42-49 as obvious over Gagnor *et al.* and Mullis *et al.* in view of Ahern *et al.* The Examiner cited Ahern as teaching the advantages of kits. Applicants respectfully traverse the rejection.

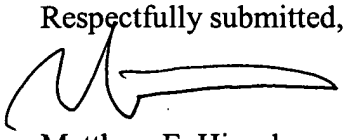
As described above, the combination of Gagnor *et al.* and Locatelli *et al.* would not result in the claimed invention. The addition of the idea of kits alone, without significantly more, does not cure the deficiencies of the other references. Accordingly, Applicants respectfully request withdrawal of the rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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